SCIENTIFIC ABSTRACT

Chronic wounds such as diabetic ulcers, pressure ulcers, and venous stasis ulcers cause significant morbidity in millions of patients each year in the US. Animal models have identified specific wound healing promoting activities of some therapeutics, and have contributed to the understanding of the pathogenesis of chronic wound. However, most therapeutic human trials have not produced clinically important results. Delivery and maintenance of the therapeutic at the wound site in sufficient quantities, and for a sufficient period of time, have been identified as major hurdles to commercialization.

A single growth factor protein, platelet-derived growth factor-BB (PDGF-BB) has been approved for use in diabetic ulcers. However, only 15% more patients treated with the approved therapeutic protein Regranex™ go on to complete healing when compared to placebo-treated patients.

GAM (gene activated matrix) technology offers the opportunity to place a therapeutic gene contained within a structural matrix into a wound site. In this proposed clinical study, the gene for PDGF-B is contained within an E1, E3 deleted adenoviral vector, which is further formulated in a bovine type I collagen gel. This type of formulation allows for the migration of wound repair cells into the structural matrix, where they encounter and internalize the viral vector, subsequently producing the therapeutic protein within this local environment.

The proposed Phase 1 study will evaluate the safety and potential clinical utility of a series of weekly topical applications (a total of four treatments), followed by multiple observations over a one year period. The primary objective of the study is to evaluate the safety of escalating doses of AdPDGF-B/GAM when delivered topically to chronic diabetic ulcers of the lower extremity. Secondary objectives are to quantitate the level of expression and transgene persistence of PDGF-BB in biopsies from treated wounds by nucleic acid testing and to obtain preliminary data about on the biological activity of AdPDGF-B/GAM.